Citation:

Braschi A, Naismith DJ. The effect of a dietary supplement of potassium chloride or potassium citrate on blood pressure in predominantly normotensive volunteers.. Br J Nutr. 2008 ;99(6):1284-92.

PubMed ID: 18053306

Study Design:

Randomized, doubleblind placebo-controlled trial with parallel arm design.

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the effect of either KCl or potassium citrate (K-cit) with a dose (30 mmol/d) approximating the current dietary deficit in the UK population and to evaluate the possible influence of the accompanying anion.

Inclusion Criteria:

Participants had to be

- aged between 22 and 65 years
- BMI between 19 and 35 kg/m^2
- an alcohol consumption of ≤ 21 units/week for women and ≤ 28 units/week for men (1 unit = 10 ml of ethanol)
- systolic BP (SBP) ≤ 160 and diastolic BP (DBP) ≤ 105mmHg at screening.

Exclusion Criteria:

- Participants suffering from postural hypotension, CVD (including cardiac arrhythmia), renal diseases, diabetes, metabolic acidosis and digestive problems or those taking anti-hypertensive medications, cyclosporin, heparin, digoxin, anticholinergics and non-steroidal anti-inflammatory drugs.
- Planning to change lifestyle, taking contraindicated medications. Aversion to BP measuring procedure, not providing urine sample and blood sample.
- Subjects who during the study period changed either their usual diet or lifestyle and those undergoing changes in psychical condition (stress, depression, tiredness) were excluded.
- Volunteers who consumed less than 80% of the placebo and data from those who consumed less than 70% during the intervention would be rejected.

Description of Study Protocol:

Recruitment

A total of 127 subjects were recruited from amongst the academic staff and the student population of King's College London. Ninety completed the study.

Design It is a randomized , doubleblind placebo-controlled trial with parallel arm design.

Blinding used (if applicable): Randomized doublind blinded placebo controlled study.

Intervention (if applicable)

- 2 week run-in with placebo capsules to test adherence and tolerance to placeboe.
- An 8-week randomized, doubleblind placebo-controlled trial with parallel arm design of oral potassium supplementation (ISRCTN no. 52748737).
- The supplement contained 5 mmol potassium microencapsulated with Eudragit NE 30 D. Two capsules were taken three times a day after each main meal (breakfast, lunch and dinner).
- Volunteers were invited to participate in a 2-week run-in period during which placebo capsules were taken in order to test adherence or intolerance to the placebo (lactose).

Statistical Analysis

- All data were checked for normality using the One-sample Kolmogorov–Smirnov test.
- The x^2 test was used to assess the significance of differences between the groups for nominal-level variables (e.g. gender).
- For interval-level variables (e.g. BP) the significance of differences between the groups at baseline was tested using ANOVA, while changes after the intervention period were tested using ANOVA with covariates (ANCOVA).
- For interval-level variables the significance of differences in parameters within each intervention group was tested by the paired sample t test (two-sided). The influence of nominallevel variables on interval-level variables was assessed using either the independent samples t test or alternatively ANOVA for more than two categories..
- Relationships between interval-level variables were examined using the Pearson correlation test (two-sided), or with the Spearman correlation test (two-sided) when non-normally distributed variables were involved.
- Data are presented as means and their standard errors.
- The increments of the parameters observed after the intervention period are presented as estimated marginal means, standard errors and 95% CI.
- A P value of ≤0·05 was considered to be statistically significant. using Minitab statistical software (version 13.1; Minitab Ltd, Coventry, UK) was used for sample size and power calculation. SPSS statistical software package SPSS 13.0 for Windows (SPSS UK Ltd, Woking, UK) was used for other calculations.

Data Collection Summary:

Timing of Measurements

- 8 weeks intervention (Baseline, mid point and final)
- At a mid-term visit BP was again measured after 3 weeks of treatment. Three days from the end of supplementation a second 24 h urine and blood sample were obtained.

Dependent Variables

- Change in:
  - blood pressure: systolic blood pressure (SBP) and diastolic blood pressure (DBP),
  - mean arterial pressure (MAP)
  - Heart rate (HR)
  - BMI (kg/m^2)
  - Urinary creatinine, K, Na, Na-K ratio

- plasma K, Na,
- haematocrit, erythrocyte water, RBC-K

Independent Variables

- potassium supplementation: potassium chloride (KCl) or potassium citrate (K-cit)

Control Variables

- SBP, DBP, heart rate, BMI, age and alcohol consumption

Description of Actual Data Sample:

Initial N: 127

Attrition (final N): 90

Age: mean (SEM) years:

- placebo (N=34): 33.8 (2.2)
- KCl (N=26): 36.9 (2.8)
- K-cit (N=30): 36.2 (2.6)

Ethnicity: UK population (Caucasian ,Middle-Eastern ,East Asian,Afro-Caribbean)

Other relevant demographics:

Across the three groups:

- 11.8% to 15.4% were vegetarians across the 3 groups (NS);
- 11.5% to 17.6% were smokers (NS);
- 30 to 44.1% had a history of familial hypertension (NS)

Anthropometrics : BMI mean (SEM):

- placebo: 22.55 (0.53)*
- KCl: 25.2 (1.06)
- K-cit: 24.5 (0.78)

* Mean values were signficantly different from those of the KCl group

Location: UK

Summary of Results:

- Mean BP was not significantly different among the three groups at baseline and throughout the duration of the study.
- Baseline SBP was significantly correlated with baseline body weight (r=0.47, P=0·000), baseline BMI (r=0.44, P=0·000), age (r=0.28, P=0·010) and alcohol consumption (r=0.24, P=0·026).
- Significant correlations were also found between DBP and baseline BMI (r=0.33, P=0·002), body weight (r=0.26, P=0·018) and age (r=0.27, P=0·012).
- At the end of the 6 week intervention period, mean BP decreased significantly from baseline within the potassium supplemented groups, while no change was observed in the placebo groups (see table)
  - After 6 weeks of supplementation, compared with the placebo group (n =31), 30 mmol K-cit/d (n =28) changed mean arterial pressure by -5.22mmHg (95% CI -8.85, -4.53) which did not differ significantly from that induced by KCl (n =26), -4.70mmHg (-6.56, -2.84).
  - The changes in systolic and diastolic BP were -6.69 (95% CI -8.85, -4.43) and -4.26 (95% CI -6.31, -2.21) mmHg with K-cit and -5.24 (95% CI -7.43, -3.06) and -4.30 (95% CI -6.39, -2.20) mmHg with KCl, and did not differ significantly between the two treatments.
- No significant relationships were found between the changes in BP and baseline BMI, age, gender, heart rate, urinary electrolyte excretion, plasma electrolytes, erythrocyte water and potassium content.
- A significant relationship (P=0·007) was found between the change in SBP (final from baseline) and SBP level (calculated as the mean of all measurements of SBP) as covariate (common slope -0·111± 0·040, intercept varies according to treatment).
- At the end of the supplementation period in the potassium groups the mean urinary excretion of potassium increased significantly from baseline.
  - The daily urinary excretion of potassium was significantly greater (P=0·010) in the K-cit (98·17 mmol/d) and KCl (89·58 mmol/d) groups than in the placebo group (66·75 mmol/d)).
  - Compared with the placebo group urinary potassium increased significantly by 24·98 mmol/d (P=0·010) in the K-cit group and by 22·60 mmol/d (P=0·010) in the

KCl group.
- After the 6-week intervention period, there were no significant changes in plasma electrolytes within the three intervention groups. Changes in plasma electrolytes did not differ significantly between the different treatments.
- There were no significant changes between and within the groups in RBC-K. After the intervention period erythrocyte water content decreased significantly in the placebo and K-cit group when compared with the respective baseline values but the changes were not significantly different between the three groups.
- Erythrocyte water content was found to be positively correlated with RBC-K (P=0·025) and plasma potassium (P=0·000).
- Changes in BP were not related to baseline urinary electrolytes. A greater treatment-related effect was observed in those with higher systolic BP.

Average blood pressure over the 6-week intervention period

	SBP			DBP			MAP		
	A	B	C	A	B	C	A	B	C
BL	107.8	111.88	114.67	66.33	68.49	70.20	80.15	82.95	85.02
MP	105.56	108.31*	110.21**	65.96	65.26	66.91	79.16	79.61*	81.35***
Final	107.80	106.39***	107.54***	66.91	64.77**	66.52***	80.54	78.64***	80.19***

Mean values were significantly different from baseline (within-group comparison):**P<0·05, **P<0·01, ***P<0·005. There were no significant differences within and between the three groups other than stated.
placebo, A; KCl, B; potassium citrate, C

Other Findings:

- There were no significant differences in mean heart rate at baseline (placebo 67·5 (SEM 1·3); KCl 67·5 (SEM 1·8); K-cit 67·8 (SEM 1·9)).
- Pulse did not change significantly within the three groups, nor did mean changes differ significantly between the groups.
- Baseline mean urinary electrolytes and creatinine excretion did not differ significantly between the three treatment groups.
- In the K-cit group the mean molar ratio of sodium to potassium (Na–K ratio) and the mean creatinine excretion decreased significantly from the respective baseline values, but these changes were not significantly different when compared with the other two groups.
- Mean BMI did not change significantly from baseline in any of the three treatments groups (placebo: 20·11 kg/m^2; KCl: 20·05 kg/m^2; K-cit: 0·11 kg/m^2) nor was the mean change in BMI significantly different between the groups.

Author Conclusion:

- Increasing dietary potassium could have a significant impact on the progressive rise in BP in the entire population
  - An increase in dietary potassium of approximately 30 mmol/d, equivalent to an increase in dietary potassium of around 40% in the UK population and to the amount contained in five portions of fresh fruits and vegetables, substantially decreases BP in predominantly young normotensive people.
  - The effect was independent of the accompanying anion of the potassium salt, was greater in those with higher BP and increased with the duration of supplementation.
  - A consistent positive correlation between BP and body weight or BMI was observed.
  - A modest increase in potassium intake, slightly exceeding the current recommendation, could make a substantial contribution to the prevention and prevalence of high BP in the UK adult population.
  - It is predicted that a reduction in BP of the magnitude observed in the present study would decrease the mortality from all forms of CVD by approximately 15%.
  - Changes in BP were not related to baseline urinary electrolytes.
  - A greater treatment-related effect was observed in those with higher systolic BP. Increasing dietary potassium could therefore have a significant impact on the progressive rise in BP in the entire population.

Reviewer Comments:

This is a randomized controlled trial . Appropriate statistical analysis was reported. Limitations of the study was also discussed in detail.

Further long term studies in prehypertension and hypertensives are required. The results suggest that there is a decrease in blood pressure which may reduce the risk of CVD. More information on dietary intakes will be helpful to assess the K intake and the source of K intakes from the diet of the population. This is not a representative sample. However the results are important because the study design is randomized and controlled parallel design.

Further studies are encouraged to see the risk reduction of CVD with reference to K supplementation.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes

10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes